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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/914,662	01/11/2002	Andreas Jordan	1214.00026	9966

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EXAMINER	
CANELLA, KAREN A	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 03/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/914,662	JORDAN, ANDREAS	
	Examiner	Art Unit	
	Karen A. Canella	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-16 is/are pending in the application.

4a) Of the above claim(s) 9-16 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-8 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 8/31/2001.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Acknowledgment is made of applicants election of Group I. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 1-16 are pending. Claims 9-16, drawn to non-elected inventions, are withdrawn from consideration. Claims 1-8 are examined on the merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(A)The term "small" in claim 1 is a relative term which renders the claim indefinite. The term "small" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Small tissue fragments can range over oders of magnitude, such as cm3 or mm3. It is unclear at what volume or size a fragment can no l;onger be considered "small".

(B)Claim 8, on page 7, recites:

Epidermal growth factor (EGF)
(Epidermal Growth Factor, EGF)
recombining 1-3000 ng/L

The significance of repeating the name of the growth factor is unclear. Further, it is unclear what action "recombining" is referred to.

(C)Claim 8, on page 7, recites:

Fetal bovine serum (FBS)

No quantity or concentration, zero or otherwise, is specified for FBS. For purpose of examination, the amount of FBS will be taken to be variable.

(D)Claims 1, 5 recite "tissue sample segments (6a)". Claim 4 recites "tissue sample (6)". The significance of (6a) and (6) is unclear.

(E)Claim 2 is vague an indefinite because it is unclear if the species of fine needle, aspiration, and intraoperative biopsies or a resection sample is referred to in the alternative. Amendment of the claim to recite "fine needle, aspiration, intraoperative biopsies or a resection sample" would overcome this rejection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2 and 5 are rejected under 35 U.S.C. 102(b) as being anticipated by Kornblith (WO 98/02038).

Claim 1 is drawn to a method of cultivating cancer cells from human tissue for molecular-biological mass screenings wherein a tissue sample is locally separated into disc segments by sequential and parallel mechanical splitting based on the heterogeneous structure of tumor cells, normal cells and contaminants, and wherein said separated tissue sample segments are further split into tissue fragments, and wherein said small, separated tissue fragments and fluids of the locally separated tissue sample segments are selectively cultivated in a specific medium and under predefined cultivation conditions and under suppression of the disturbing influence of normal cells and contaminants. Claim 2 embodies the method of claim 1 wherein said tissue sample is obtained from fine needle, aspiration and intraoperative biopsies or a resection sample. Claim 5 embodies the method of claim 1 wherein the tissue fragments and fluids obtained from the locally separated tissue sample segments are cultivated separately in tissue culture bottles filled with said medium and coated with a biomatrix substrate in an 0.01% to 3% oxygen atmosphere, an 0.1% to 5% CO3 atmosphere at a humidity of 100% and

temperature in the range from 30-36.5 degrees C. Claim 6 embodies the method of claim 5 wherein the medium in the culture bottle is replaced by fresh medium of the same composition some time after initial establishment of the cell culture and completed adhesion.

Kornblith discloses a method for screening a multiple of candidate therapeutic or chemotherapeutic agents for efficacy as to a specific patient, in which a tissue sample from the patient is harvested, cultured and separately exposed to a plurality of treatments and/or therapeutic agents for the purpose of objectively identifying the best treatment for the cultured cells obtained from the patient (page 2, lines 28-35). Kornblith discloses that a particularly important tissue sample preparation technique is the initial preparation of cohesive multicellular particulates of the tissue sample, rather than enzymatically dissociated cell suspensions or preparations, for initial tissue culture monolayer preparation and that by maintaining malignant cells within a multicellular particulate of the originating tissue, growth of the malignant cells themselves is facilitated versus the overgrowth of fibroblasts or other cells which tends to occur when suspended tumor cells are grown in culture (page 3, lines 2-14). Kornblith discloses that practical monolayers of cells may thus be formed to enable meaningful screening of a plurality of treatments and/or agents (page 3, lines 20-23).

Kornblith discloses that the sample is a tumor biopsy of > 100 mg of nonnecrotic, non-contaminated tissue is harvested from the patient by any suitable biopsy or surgical procedure known in the art (page 4, lines 30-35). Kornblith discloses that the tumor is removed, under sterile conditions, from the shipping container and is minced with sterile scissors but if f the specimen arrives already minced, the individual tumor pieces should be divided into four groups (page 5, lines 2-6). Kornblith discloses that each undivided tissue quarter is then placed in 3 ml sterile growth medium (Standard F-10 medium containing 17% calf serum and a standard amount of Penicillin and Streptomycin) and systematically minced by using two sterile scalpels in a scissor-like motion, or mechanically equivalent manual or automated opposing incisor blades and that said cross-cutting motion is important because the technique creates smooth cut edges on the resulting tumor multicellular particulates (page 5, lines 6-15). Kornblith discloses that preferably the tumor particulates each measure 1 mm3 and that after each tumor quarter has been minced, the particles are plated in culture flasks using sterile pasteur pipettes (9 explants per T-25 or 20 particulates per T-75 flask, page 5, lines 15-19). Kornblith discloses that the

explants should be evenly distributed across the bottom surface of the flask, with initial inverted incubation in a 37 degree C. incubator for 5-10 minutes, followed by addition of about 5-10 ml sterile growth medium and further incubation in the normal, non-inverted position (page 5, lines 21-26). Kornblith teaches that the flasks should be checked daily for growth and contamination and weekly removal and replacement of 5 ml of growth medium (page 5, lines 27-28). Kornblith discloses that the flasks are placed in a 35 degree C, non-CO2 incubator (page 5, lines 26-29) which fulfills the specific embodiments of claim 5. The disclosure of Kornblith fulfills the specific embodiments of cultivation of separated tissue fragments and fluids because the mincing of the tissue segment while in sterile growth medium, and the propagation of the initial culture from said medium would inherently comprise any fluids from the locally separated tissue sample segment. The disclosure of Kornblith fulfills the specific embodiments of cultivation under suppression of the disturbing influences of normal cells and contaminants because Kornblith discloses that the growth of the malignant cells is facilitated versus the overgrowth of fibroblasts or other cells which tends to occur when suspended tumor cells are grown in culture, therefore the growth of the undesired cells is suppressed. The disclosure of Kornblith anticipates the specific embodiments of claims 5 and 6 because Kornblith directs the inspection of the flasks for microbial contamination, and the weekly replacement of the growth medium.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-3 and 5-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kornblith (WO 98/02038) in view of Freshney (Culture of Animal Cells, 3rd Ed., 1994, page 264).

Claim 3 embodies the method of claim 2 wherein the culture medium for storage of freshly taken sample and the medium to be used for cultivating the tumor cells are identical.

The teachings of Kornblith on the specific embodiments which anticipate claims 1, 2, 5 and 6 are set forth above. Kornblith does not specifically teach that the transport medium and the cultivation medium are the same.

Freshney teaches that cells may be transported in medium (page 264, second column, lines 3-8).

It would have been prima facie obvious at the time the claimed invention was made to provide the surgeon with medium that would be used for cultivation so that the biopsy sample(s) may be transported in said medium. One of skill in the art would be motivated to do so in order that all samples collected from various sources would be exposed to the same nutrient conditions ex vivo. One of skill in the art would also be motivated to do so in order that the tumor sample would not undergo two separate adjustments to osmolality, pH and nutrients in two different media. One of skill in the art would be motivated to try to preserve the viability of the tumor specimen. Further it would be prima facie obvious to replace the medium

Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Freshney (Culture of Animal Cells, 3rd Ed., 1994, pp. 84-100).

Claim 8 is drawn to a cell culture medium comprising the ingredients listed on pages 4-7 of the claims. It is noted that the intended use of said medium does not provide patentable distinctness over prior art product.

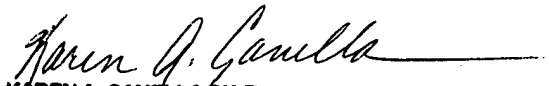
Freshney teaches the constituents of different types of media which have constituents that fall within the claimed ranges (pages 84-99). Freshney teaches that the choice of medium and serum is either empirical or by comparative testing of several media (page 99, first column, lines 6-7 under heading). It would be prima facie obvious to one of skill in the art at the time the claimed invention was made to optimize the concentration of salts, amino acids, vitamins, glucose, hormones and growth factors. One of skill in the art would have been motivated to do so by the teachings of Freshney that the choice of medium and serum requires testing on the actual cells to be cultivated.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 10 a.m. to 9 p.m. M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on (571)272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Karen A. Canella, Ph.D.
3/21/2005



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PRIMARY EXAMINER